Intra-Ocular Injections of Solutions of Various Antiseptic Substances; An Experimental Inquiry.

Read in the Section on Ophthalmology at the Forty-Fourth Annual Meeting of the American Medical Association.

BY G. E. DE SCHWEINITZ, M.D.

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INTRA-OCULAR INJECTIONS OF SOLUTIONS OF VARIOUS ANTISEPTIC SUBSTANCES; AN EXPERIMENTAL INQUIRY.

A number of researches have been published concerning the effect of the introduction of various substances, solid and liquid, into the vitreous chamber. These may be summarized as follows:

1. The introduction into the vitreous of foreign bodies (pieces of wire, lead, glass, etc.), or of irritating liquids (croton oil, tincture of iodin, etc); 2, the injection of sterilized blood into the vitreous humor; 3, intra-ocular injections of various antiseptic liquids.[1]

Researches belonging to the first class, from the time of the publication of Pagenstecher's essay on the pathology of the vitreous[2] to Leber's superb work,[3] are chiefly concerned with the behavior of the vitreous towards these foreign substances, and with the complex problems which surround the pathology of inflammation.

Researches of the second class, which date from the imperfect experiments of Legros,[4] to the thorough investigation of the subject of blood injections into the vitreous by Pröbsting,[5] have been undertaken to study the deportment of the retina under these circumstances, and to add to our knowledge of the

[1] Experiments to determine the effects of injections into the anterior chamber, for example those performed by Nuel (Revue Générale d'Ophtalmologie, T. viii, 1889, p. 343) do not belong to the present classification. As Dr. Berry points out, injections into the anterior chamber and into the vitreous can scarcely be compared.

[2] Archives of Ophthalmology, Vol. I, p. 500.

[3] Die Enstehung der Entzündung und die Wirkung der Entzündungerregenden Schädlichkeiten. Leipzig, 1891, p. 177 et seq.

[4] Journal de la Anatomie et de la Physiologie, 1873.

[5] Archiv f. Ophtalmologie, Bd. xxxviii, Abt. III, 1892, p. 114.

mechanism of retinal detachment and the production of proliferating retinitis.

Researches of the third class have been conducted chiefly to test the therapeutic value of the injection of antiseptic fluids directly into the vitreous of an inflamed eye, for example, one suffering from hyalitis, or from sympathetic ophthalmitis; or to try their efficacy in preventing an inflammation of this character after the eye has been exposed to the influences likely to produce it.

Abadie,[6] in 1890, suggested the propriety of injecting 2 drops of a solution of sublimate, 1 to 1000, into a wounded eye, causing sympathetic ophthalmitis of the other eye, which in turn should also be treated with a similar injection directly into the vitreous humor. According to him, these injections were of use in checking and ameliorating the inflammatory process. Subsequently he published[7] three cases of sympathetic ophthalmitis cured by intra-ocular injections of corrosive sublimate, the strength of the injections being in two instances, 1 to 1000, and in one, 1 to 500.

In the discussion of a paper communicated by Darier, Abadie's Chief of Clinic, to the French Society of Ophthalmology, on the 8th of May, 1891,[8] concerning sub-conjunctival injections of sublimate in ocular therapeutics, the question of intra-ocular injections of the same drug received attention, Wecker regarding the transition from intra-ocular to sub conjunctival injections as a decided advance, and doubting the efficacy of the former method of administration. In the close of the discussion, Abadie expressed himself as willing to abandon the intra-ocular injections of sublimate for sub-conjunctival injections, provided it is demonstrated that

[6] Pathogénie et nouveau Traitement de l'Ophthalmie Sympathetique. Annales d'Oculistique, Vol. ciii, 1890, p. 183.

[7] Nouveaux cas d'Ophthalmie Sympathique, Guéri par les Injections intra-oculaires de Sublimé. Annales d'Oculistique, Vol. civ, 1890, p. 229.

[8] Des Injections sous—conjunctivales de Sublimé en Thérapeutique oculaire, Arch. d'Ophthal. Vol. xi, 1891 p. 449.

they are more efficacious, inasmuch as certain observers have doubted their efficacy and, moreover, have not merely been disappointed in their results, but have seen positive harm follow. Still later* he asserts that although sub-conjunctival injections are preferable in most cases, intra-ocular medication of this character must not be entirely abandoned.

Occasionally reports of successes from the use of Abadie's treatment of migratory ophthalmitis have appeared in the journals; for example, Baquis[9] reports a remarkable case of this character: a woman aged 26 years sustained an injury of the left eye, resulting in an adherent leucoma. At the end of three months chronic irido-cyclitis produced sympathetic ophthalmitis in the left eye. The author then injected 3 drops of a sublimate lotion, 1 to 500, into the sympathizing eye. Marked improvement occurred. At the end of eight days the injection was repeated, but there were also twelve mercurial frictions, which caused the absorption of the exudates in the pupillary field, and revealed an intense neuro-retinitis in the sympathizing eye. At the end of six months the cure continued. This author states that he was encouraged to use Abadie's method, not only by the results obtained by the reporter, but on account of the researches of Dr. Ovio of Padua, on the intra-ocular circulation and the nutrition of the vitreous. The latter experimenter definitely asserts that weak sublimate lotions may be injected into the vitreous without creating chronic lesions, diminishing the micro-bicidic power of the sublimate lotions, no matter how weak they may be.

Darier[10] states that he experimented in 1889, on rabbits with the intra-ocular injections of "various substances," and that in studying daily the mod-

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*Annales d'Oculistique, August, 1893.

[9] Annali di Ottalmologia, Vol. xxi, fasc. 4 et 5, Abstr. Arch. d'Oph. December, 1892, p. 781.

[10] Des Injections sous—conjunctivales de Sublimé. Annales d'Oculistique, T. civ., Avril, 1893, p. 242.

ifications produced by the substances on the vitreous body and the deep membranes of the eye, he was struck by observing how promptly the solutions thus introduced were absorbed without causing excessive disturbance, provided they were very dilute. The character of the substances is not described in the paper to which reference has been made.

At a meeting of the Ophthalmological Society of the United Kingdom, Nov. 10, 1892, Berry[11] gave an account of some facts elicited by experiments on rabbits, undertaken by his assistant, Dr. Chassaud, with the object of ascertaining the effect of different solutions injected into the vitreous. Unfortunately the details of these experiments are not at hand, but in the abstract given the following results are recorded: in some cases, before injecting the antiseptic, the vitreous was inoculated with fresh septic pus. The only substance injected after inoculation which seemed capable of preventing purulent hyalitis was chlorine water, and this injection was better tolerated by the retina and vitreous than other strong antiseptic fluids. In two cases of purulent hyalitis in man, chlorine water injected into the vitreous led to immediate improvement and the eyes were saved, although sight had been lost before treatment was adopted. In the discussion which followed, Griffith suggested the propriety of the use of trichloride of iodine as an intra-ocular injection—an antiseptic, as is well known, which has been much lauded by Pflüger and others in France. Berry expressed the belief that the use of intra-ocular injections was a distinct advance in ocular therapeusis, and Mr. Hartridge, referring to cases in which the injection of a germicidal solution was evidently indicated, thought that if this method could be demonstrated to be a safe one, a very desirable addition to ocular therapeutics would be made.

[11] Intra-ocular Injections of Antiseptic Solutions. Ophthalmic Review, December, 1892.

Therefore, both from the clinical and the experimental standpoint, it is desirable to add new data. Those which I present are entirely experimental and comprise:

1. The injection of various antiseptic substances into the vitreous chamber of rabbits, namely, bichloride of mercury, 1 to 500, 1 to 1,000 and 1 to 5,000 respectively; cyanuret of mercury, 1 to 1,000; aqua chlorinata, officinal strength; blue pyoktanin, 1 to 1,000 and trichloride of iodine 1 to 1,000.

2. The injection into the vitreous chamber (dogs and rabbits) of an emulsion of staphylococcus pyogenes aureus of the sixth generation, and after the development of purulent hyalitis the injection of antiseptic fluids (bichloride of mercury and aqua chlorinata).

3. The simultaneous injection of the staphylococcus emulsion aud the antiseptic fluids.

FIRST SERIES.

Experiment 1.—2, 8, 1893. Full grown, slate-colored rabbit. Five minims of bichloride of mercury solution, 1 to 500, injected into the vitreous. 2, 9, 1893. Vitreous cloudy, and at the upper portion somewhat in the position of the injection, a large, dark cloud and a smaller detached one lower down. 2, 20, 1893. No change in the permanent lesion of the vitreous.

Experiment 2.—2, 17, 1893. Full grown, black rabbit. Five minims of bichloride of mercury, 1 to 1,000, injected into the right vitreous; 2, 20, 1893. Vitreous cloudy. 2, 24, 1893. Vitreous entirely opaque; practically no reflex from the fundus; 3, 1, 1893. Rabbit killed and eye placed in Müller's fluid.

Microscope.—Choroid edematous; retina practically indistinguishable, being merged into a tissue composed of round and oval cells, well developed fibers and blood channels, through the outer layers of which are freely scattered oval and round, densely pigmented cells. Additional areas of blood corpuscles and patches of granular débris are visible.

Experiment 3.—2, 17, 1893. Full grown, white-nosed Maltese rabbit. Five minims of bichloride of mercury, 1 to 1,000, injected into the right vitreous. 2, 20, 1893. Large, greenish-white cloud occupying vitreous. 2, 24, 1893. Similar appearances, giving somewhat those presented by connective tissue formation in vitreous. 3, 6, 1893. Eye removed and

placed in Müller's fluid. Ophthalmoscopically the vitreous was occupied by a huge whitish mass covered with reddish spots, probably hemorrhages, and giving the impression of extensive detachment of the retina.

Microscope.—Fine granular débris in anterior chamber; remains of vitreous granular, but no connective tissue ormation. Choroid imperfect and detached (section, however, broken somewhat, hence possible fault in technique); retina extensively detached, in places normal in structure, but in others proliferation of Mueller's fibers (connective tissue framework) passing into vitreous and forming a delicate network of fine fibers. (Compare results obtained by Pröbsting, loc. cit. page 139.) The lesions are analogous to proliferating retinitis.

Experiment 4.—2, 17, 1893. Full grown, gray rabbit. Five minims of bichloride of mercury, 1 to 5,000, injected into the right vitreous. 2, 20, 1893. Large, dark cloud occupying vitreous. No change before rabbit's death, four days later.

Experiment 5.—5, 5, 1893. Full grown, buff-colored rabbit. Two minims of bichloride of mercury, 1 to 500, injected into left vitreous. Immediately afterwards two air bubbles and a small circular cloud visible with ophthalmoscope. 5, 9, 1893. Dark opacity in the vitreous up and out, stationary, and resembling a fly's wing. The rest of the vitreous clear. 5, 11, 1893. Opacity in the vitreous unchanged. 5, 17, 1893. Previously described opacity remains stationary. Slight general haze in the vitreous. 5, 29, 1893. Rabbit dead. No change in the opacity.

Experiment 6.—Large, buff-colored rabbit (pregnant). Two drops of bichloride of mercury, 1 to 500, injected into the left vitreous. Immediately afterwards a dark streak marking the track of the needle; a small dark cloud just in the center of the vitreous. 5, 9, 1893. Circular opacity in the vitreous with small, central spot. The rest of the vitreous clear. 5, 11, 1893. The large circular opacity, with a smaller dark center described in previous note unchanged. The remainder of the vitreous clear. 5, 17, 1893. Opacity in the vitreous of dense white color, shaped like two superimposed rings; rest of vitreous clear. 6. 1, 1893. No change in previously described opacities. Rabbit killed and eye placed in Müller's fluid; not yet examined.

Experiment 7.—2, 17, 1893. Full grown, black rabbit. Ten minims of aqua chlorinata injected into left vitreous. On withdrawing syringe a large bleb appeared beneath the conjunctiva, and the vitreous seemed to be filled with a cloudy substance and several air bubbles. 3, 6, 1893. Extensive clouding of the vitreous, with probable detachment of the retina. 3, 20, 1893. Eye placed in Müller's fluid; no change, other than deepening of opacity, having occurred.

Microscope.—Choroid for the most part in place, but

edematous; prolapse at point of entrance of needle. Retina extensively detached and scarcely recognizable, being associated with a band of connective tissue and round and oval cells, and inflammatory material extending from nerve entrance to anterior portion of eye.

Experiment 8.—2, 17, 1893. Full grown, white-nosed Maltese rabbit. Ten minims of aqua chlorinata injected into left vitreous. 3, 6, 1893. Vitreous has remained clear; that is, there have been no dark opacities or white infiltrations, and the eyeground is visible without apparent change in the retina. 3, 20, 93. Eye placed in Müller's fluid, but not yet examined.

Experiment 9.—2, 17, 1893. Full grown, gray rabbit. Ten minims of aqua chlorinata injected into left vitreous. 3, 6, 93. Extensive white clouding of the vitreous, and probable detachment of the retina. 3, 20, 1893. Eye placed in Müller's fluid, but not yet examined.

Experiment 10.—3, 8, 1893. Full grown, white and gray rabbit. Ten minims of aqua chlorinata injected into right vitreous. 3, 11, 1893. Cornea hazy and no view of fundus. (Probable contamination from imperfect sterilization of needle.)

Experiment 11.—3, 8, 1893. Full grown white and gray rabbit. Five minims of aqua chlorinata injected into right vitreous. 3, 11, 1893. Large, greenish-white opacity well forward in the vitreous, giving the appearance of an old detachment of the retina, and connective tissue formation in vitreous. No change before rabbit's death, three days later.

Experiment 12.—3, 8, 1893 Full grown white and gray rabbit. Ten minims of aqua chlorinata injected into right vitreous. 3, 11, 1893. Large greenish-white opacity obscuring the entire vitreous. Eye removed and placed in Müller's fluid.

Microscope.—Retina and choroid for the most part in place and of fairly normal appearance, but well forward on right side a circumscribed detachment of retina, the space between retina and choroid being filled with a granular material (coagulated vitreous) containing a number of hypertrophied vitreous cells.

Experiment 13.—4, 17, 1893. Full grown black rabbit. Ten minims of aqua chlorinata injected into right vitreous. Immediately afterwards a large air bubble surrounded by a dark cloud. 4, 20, 1893. Circular white opacities and still some air bubbles present in the vitreous. 4, 28, 1893. Several large, white opacities hanging in the vitreous surrounded, however, by clear vitreous, permitting a view of the fundus. No hemorrhages in the retina and no detachment. 5, 9, 1893. Practically no change from note under 4, 28, 1893. 5, 17, 1893. Irregular, dense, white opacities scattered

throughout the retina, between which the fundus is dimly seen, with evident patches of choroiditis down and out. 6, 1, 1893. No change from above. Eye removed and placed in Müller's fluid, but not yet examined.

Experiment 14.—4, 17, 1893. Full grown black rabbit. Ten minims of aqua chlorinata injected into right vitreous. Immediately afterwards numerous air bubbles surrounded by a cloud. 4, 20, 1893. Streaks of dark opacity and clouding of the vitreous, partially obscuring the fundus. 5, 4, 1993. Entire vitreous opaque and whitish. Lens beginning to be cataractous. 5, 9, 1893. Diffuse opacity of the entire vitreous, presenting the general appearance of a white cataract. 5, 11, 1893. Eye removed and placed in boro-glyceride, but not yet examined.

Experiment 15.—2, 20, 1893. Full grown white and gray rabbit. Five minims of cyanuret of mercury, 1 to 1,000, injected into right vitreous. 2, 24, 1893. Vitreous cloudy and eye-ground invisible. No change before rabbit's death.

Experiment 16.—2, 20, 1893. Full grown white and gray rabbit. Five minims of cyanuret of mercury, 1 to 1,000, injected into right vitreous. 2, 24, 1893. Vitreous cloudy and streaked, but appearances of whitish masses and detachment of the retina lacking. No clearing of vitreous before the rabbit's death, three days later.

Experiment 17.—Five minims of cyanuret of mercury, 1 to 1,000, injected into left vitreous. Immediately afterwards dark streaks in vitreous and several air bubbles. 3, 11, 1893. Vessels of the retina visible, but the vitreous hazy and streaked. Rabbit dead two days later, without change.

Experiment 18.—3, 8, 1893. Five minims of cyanuret of mercury, 1 to 1,000, injected into left vitreous. Immediately afterwards dark streaks in vitreous and several air bubbles. 3, 11, 1893. Vitreous shows large, greenish-white opacity obscuring the fundus. Eye removed and placed in Müller's fluid.

Microscope.—Choroid edematous; retina much broken and detached; typical prolapse of choroid into wound made by entrance of needle. The internal portion of the puncture is closed with granular pigment cells from the choroid; beyond is a tissue composed of round and oval cells (granulation tissue) capped at the scleral orifice with pigment granules.

Experiment 19.—3, 8, 1893. Full grown gray and white rabbit. Exact repetition of Experiment 16.

Experiment 20.—4, 17, 1893. Full grown black rabbit. Five minims of cyanuret of mercury, 1 to 1,000, injected into left vitreous. Immediately afterwards a large air bubble surrounded by a dark cloud. 4, 20, 1893. Whitish and darkish opacities in the vitreous partially obscuring the retina. 4, 28, 1893. Vitreous opaque and whitish. 5, 9, 1893. Scattered

whitish opacities throughout the vitreous obscuring any view of the fundus. 5, 17, 1893. Entire vitreous opaque, of a dense white color.

Experiment 21.—4, 17, 1893. Full grown black rabbit. Five minims of cyanuret of mercury, 1 to 1000, injected into left vitreous. 4, 20, 1893. Whitish and grayish opacities in vitreous, largely obscuring the retina. 4, 28, 1893. Entire vitreous filled with an irregular whitish mass covered with hemorrhages. 5, 9, 1893. Practically no change from note under 4, 28, 1893, except that in the upper and inner portion of the vitreous there is a break in the opacity, permitting a red reflex from the fundus. 5, 11, 1893. Eye removed and placed in Müller's fluid.

Microscope.—Choroid detached; retina not distinguishable, being bound up with extensive tissue formation in vitreous composed of young fibrous tissue, inflammatory cells, pigment cells and blood corpuscles.

Experiment 22.—5, 11, 1893. Large buff-colored rabbit (pregnant). Two minims of trichloride of iodin injected into right vitreous. Immediately afterwards two air bubbles and a small ring of opacity visible with the ophthalmoscope. 5, 17, 1893. Large circular opacity of dense white color with a clear center directly in the center of the vitreous; the rest of the vitreous clear. 6, 1, 1893. Circular opacity described above, with strands of similar color passing in several directions through vitreous. Eye removed and placed in Müller's fluid, but not yet examined.

Experiment 23.—5, 11, 1893. Full grown buff-colored rabbit. Five minims of blue pyoktanin, 1-1000, injected into right vitreous. Immediately afterwards a small purple cloud visible in the center of the vitreous. 5, 17, 1893. Irregular dark opacity up and in, and the entire vitreous of a faint, purplish hue. No detachment of the retina. 6, 1, 1893. No change before rabbit's death, two days ago.

SECOND SERIES.

Experiment 1.—2, 8, 1893. Full grown albino rabbit. Two minims of an emulsion of staphylococcus pyogenes aureus of the sixth generation injected into right vitreous. 2, 9, 1893. Some purulent conjunctivitis, entire cornea hazy, iris dimly visible below; in the upper and inner portion of the cornea a yellowish, purulent mass. Five minims of bichloride of mercury 1-500 injected directly into the vitreous. 2, 10, 1893. Much increase in the purulent keratitis. Eyeballs soft. Germicidal injection repeated. 2, 17, 1893. Rabbit dead from general infection.

Experiment 2.—2, 24, 1893. Full grown white and gray rabbit. Production of extensive hypopyon keratitis and probably purulent hyalitis by emulsion of staphylococcus. Five

minims of bichloride of mercury 1-5000 injected without result. Rabbit dead from general infection.

Experiment 3.—2, 8, 1893. Large mongrel poodle, full grown. Five minims of emulsion of staphylococcus injected into right vitreous. 2, 9, 1893. Slight conjunctivitis, cornea hazy and pus in the central layers. No view of fundus. Ten minims of bichloride of mercury 1-500 injected into vitreous. 2, 10, 1893. Extensive purulent keratitis, the eye soft, injected, and apparently in a state of panophthalmitis. Germicidal injection repeated. 3, 8, 1893. No further treatment was given to the mongrel poodle except to wash his eye with warm water. The conjunctivitis gradually disappeared and the eyeball lost its inflammation. At this date the eye is quiet, slight injection of the episcleral vessels, no pus anywhere visible, the cornea hazy in its lower portion, but the iris visible above, being a result entirely unexpected after the injection of the staphylococcus.

Experiment 4.—2, 20, 1893. Gray and white rabbit. Five minims of staphylococcus emulsion injected into right vitreous. 2, 21, 1893. Five minims of bichloride of mercury, 1-500, injected. 2, 24, 1893. Purulent ulcer and hypopyon and the rabbit dead of general infection.

Experiment 5.—2, 20, 1893. Full grown rabbit. Exact repetition of Experiment 4, with the same result.

THIRD SERIES.

Experiment 1.—2, 27, 1893. Full grown black rabbit. Five minims of staphylococcus emulsion injected into right vitreous, immediately followed by 5 minims of bichloride of mercury, 1-500. 3, 1, 1893. Cornea infiltrated and a large quantity of pus in its lower portion. 3, 6, 1893. Entire cornea red, pus filling the anterior chamber. 3. 10, 1893. Eye intensely hyperemic; extensive hypopyon. No ultimate improvement.

Experiment 2.—2, 27, 1893. Full grown tan and white rabbit. Five minims of staphylococcus emulsion injected into right vitreous, immediately followed by 10 minims of cyanuret of mercury, 1-1000 3, 1, 1893. Cornea cloudy and infiltrated. No view of the eye ground. 3, 6, 1893. Large mass of the appearance of lymph filling the anterior chamber and giving the impression of spongy iritis. 3, 10, 1893. Extensive hypopyon keratitis with purulent conjunctivitis. No ultimate improvement.

Experiment 3.—2, 27, 1893. Full grown gray rabbit. Two minims of staphylococcus emulsion, immediately followed by an injection of 10 minims of aqua chlorinata, into the right eye. 3, 6, 1893. Hypopyon keratitis. 3, 10, 1893. Entire cornea cloudy and infiltrated, and pus filling the entire anterior chamber. Eyeball removed and placed in Müller's fluid.

The thirty-one experiments which comprise this research may be summarized as follows:

Normal Eyes.—There were six injections with bichloride of mercury, the dose varying from 2 to 10 minims; in all, permanent lesions visible with the ophthalmoscope were produced in the vitreous; two eyes examined with the microscope showed extensive new formed connective tissue in the vitreous, together with detachment of the choroid and retina on the one hand, and on the other, lesions indicating an early stage of proliferating retinitis.

There were eight injections with aqua chlorinata, the dose varying from 5 to 10 minims; in all, permanent vitreous lesions were produced, except in one (Experiment 8), in which the vitreous remained clear; that is, there were no well-formed dark opacities, or white areas of infiltration. One eye in this series was contaminated by imperfect sterilization of the syringe. Two eyes were examined with the microscope, and showed in one, after thirty-one days had elapsed, extensive detachment of the retina and the formation of a band of tissue composed of young cells and fibers constituting the so-called inflammatory material, which passed from the optic nerve entrance through the entire vitreous; and in the other, a circumscribed detachment of the retina three days after the injection.

There were eight injections with cyanuret of mercury, the dose being 5 minims in each, and causing in every instance positive lesions in the vitreous demonstrable with the ophthalmoscope in the form of more or less dense opacities. Two eyes examined with the microscope showed in one detachment of the retina, hernia of the choroid into the wound produced by the puncture with the needle, causing traction on this membrane; and in the other, twenty-five days after injection, extensive tissue formation in the vitreous of the type previously described.

There was one injection of trichloride of iodine, the dose being 2 minims, resulting in dense opacity of

the vitreous. There was one injection of blue pyoktanin, resulting in a purplish discoloration of the vitreous, and a cloud-like opacity.

Pathological Eyes.—In the first series there were five experiments—four rabbits and one dog—purulent hyalitis going on to purulent ophthalmitis, having been produced by staphylococcus emulsion. The inflamed eyes were treated by injections of bichloride of mercury directly into the vitreous, the dose being 5 and 10 minims, and varying in strength from 1-500 to 1-5000. The rabbits failed to show any signs of amelioration, and died from general infection. The dog showed no improvement at first but gradually improved, and one month after the last injection, only two having been given, was discharged with the eye comparatively quiet, a moderately dense macula being all that remained of an inflammation which at its height gave evidence of the most extensive purulent kerato-iritis, probably ophthalmitis.

In the second series there are three experiments, all rabbits, who received a simultaneous injection of staphylococcus emulsion and 5 minims of bichloride of mercury 1-500, 10 minims of cyanuret of mercury 1-1000, and 10 minims of aqua chlorinata, officinal strength, respectively. In no case was there the slightest improvement. The eyeball of Experiment 3, treated with aqua chlorinata, was examined with the microscope and showed purulent infiltration of all of the coats of the eye—in other words, an acute panophthalmitis.

It is evident that in the normal eyes injected with solutions of various antiseptic substances, only one escaped positive permanent lesion easily visible with the ophthalmoscope, and situated usually in the vitreous, more rarely in the choroid and retina. This exception occurred with aqua chlorinata, and is so unexpected a result that suspicion is not lacking that there may have been failure to introduce the drug as thoroughly as in the other eyes, although there is no note as to any imperfection in the experiment. It is

mentioned, however, because, as will be remembered, Dr. Berry has found that chlorine water was better tolerated by the retina and vitreous than other strong antiseptic fluids.

These experiments certainly fail to confirm the observations of Ovio, that weak solutions of sublimate may be injected into the vitreous without causing chronic lesions; that is to say, a solution of 1-5000 will produce as much disturbance as a lotion of 1-500. It seems evident from the experiments that under any circumstance more would depend upon the dose of the drug injected than upon the strength of the solution used. Two minims seem to be much less likely to cause a general clouding of the vitreous than 5 or more minims, but none the less, even in this small dose, in each instance they caused a dense vitreous opacity. In addition to the lesions which were so evident with the ophthalmoscope, the microscope shows that they were not confined alone to the vitreous, and that others, not ordinarily detectable, were present. Thus, according to circumstances, we deal with edema and rarefaction of the choroid; sometimes with its detachment; with detachment of the retina and a type of retinitis analogous to that which is designated proliferans; and with connective tissue formation in the vitreous of extensive character. Not only this, but it is interesting to note that in two of the punctures examined there was well-marked hernia of the choroid. How much such incarceration of this membrane would add to the danger of the treatment it is difficult to decide. It is suggestive of the fact that other punctures in operative surgery in this region may be followed by a similar result.

The entire failure to check the purulent inflammation called into existence by staphylococci emulsion, by injecting into the vitreous strong solutions of bichloride of mercury, or to prevent its occurrence by a simultaneous injection of a solution of bichloride of mercury, cyanuret of mercury, or aqua chlorinata, is

instructive, as showing an indifferent therapeutic power on the part of these injections; but it should be remembered in all fairness, that the inflammation was exceedingly active, that the number of experiments is comparatively few, and that the animals used were rabbits, whose well-known susceptibility to all agents which cause suppuration renders them peculiarly liable to the activities of the staphylococci, and equally difficult to impress with counteracting remedies. The apparent cure of the mongrel cur is interesting as an isolated fact, but can not be accepted in confirmation of the value of the treatment chiefly because it is a single experiment and needs repetition. In fact, to test the therapeutic value of these injections, dogs should be submitted to a similar series of experiments.

The conclusion of the whole matter, from the standpoint of the present research, evidently is, that the vitreous, choroid and retina withstand badly intra-ocular injections of various antiseptic solutions; that these injections in rabbits have no influence in preventing or checking a purulent inflammation originated by staphylococci injection; that if the drugs are to be employed for this purpose, the dose should be a small one, probably not more than 2 minims, according to Abadie's original recommendation. Before accepting this method of medication, even within the limits specified, much additional knowledge is needed in regard to the exact therapeutic relation of these fluids, when introduced into the eye, to a microbic disease, and especially the relation of the chemical composition of the vitreous to that of the fluid injected.